UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,521	11/15/2005	Dominique Bernard	1032487-000010	9358

21839 7590 06/01/2007
BUCHANAN, INGERSOLL & ROONEY PC
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
06/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,521	BERNARD ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2007*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,28-36 and 46-52* is/are pending in the application.

4a) Of the above claim(s) *36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,28,35 and 48-52* is/are rejected.

7)☒ Claim(s) *29-34,46,47 and 52* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/7/05;4/20/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *sequence match*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-11, 28-35, 46 and 47, and SEQ ID NO:6 in the response to restriction requirement and amendment filed March 8, 2007 are acknowledged. In the amendment, new claims 48-52 have been added. The traversal is on the ground(s) that Groups I and II are both endowed with properties to target SASPase for improving skin conditions and are related to the same polypeptide sequences, and there is no lack of unity of invention in the PCT search report issued during the international phase of this application; and the same argument also applies to the sequence election among various SASPase polypeptides. Applicants' response has been considered, however, the arguments are not found persuasive because each Group is directed to a distinct chemical entity (i.e., proteins or antibodies) and/or methods which use different materials and produce different effects, e.g., Group I is directed to a SASPase polypeptide, a pharmaceutical or cosmetic composition comprising the SASPase polypeptide and a method of treating a skin condidition associated with dysfunction of cell proliferation and differentiation by administering the composition, while Group II is directed to a monoclonal or polyclonal antibody, which specifically recognize the SASPase polypeptide. These two groups are patentably distinct because the antibody, which is structurally and functionally different from SASPase polypeptide and has different utility, e.g., the antibody of Group II cannot be used in the method of Group I. Regarding various sequences of SASPase polypeptides, since each polypeptide has different amino acid sequence and different chemical and physical properties, they are patentably distinct from each other. Furthermore, additional sequence search for extra claimed amino acid sequences would add serious search

burden on the examiner. Accordingly, the claims are not so linked by a special technical feature within the meaning of PCT Rule 13.2 so as to form a single inventive concept and lack of unity is deemed proper.

Since the peptide sequences of SEQ ID NO:4 and 5 comprises the sequence of SEQ ID NO: 6, upon reconsideration, these two sequences are joined with SEQ ID NO:6 for examination. Therefore, claims 1-11, 28-35 and 46-52, and SEQ ID NO:4, 5 and 6 are examined; claim 36 and SEQ ID NOs: 1, 7, 8, 9, 16, 25 and 27 non-elected inventions and withdrawn from consideration.

Informalities

The disclosure is objected to because of the following informalities:

2. Fig. 4 contains two amino acid sequences, however, the brief description of Fig. 4 (at page 28) does not identify these sequences with sequence identifier "SEQ ID NO:". Appropriate correction is required.

Claim Objections

3. Claims 1-11, 28-35, 46 and 47 are objected to because the claim contains non-elected sequences.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 7-11, 50 and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is not enabling for a method for combating skin conditions associated with a dysfunction of cell proliferation and/or differentiation or treating a dermatological infection, comprising administering the composition comprising an effective amount of at least one polypeptide of SEQ ID NO:4, 5 or 6, homologs thereof, or a mixture derived from the proteolysis of the polypeptide.

Claims 7-11, 50 and 51 are directed to a method for combating skin conditions associated with a dysfunction of cell proliferation and/or differentiation or treating a dermatological infection, comprising administering the composition comprising an effective amount of at least one polypeptide of SEQ ID NO:4, 5 or 6, homologs thereof, or a mixture derived from the proteolysis of the polypeptide. The specification, however, only discloses cursory conclusions (pages 15-16) without data supporting the findings, which state that the invention relates to a composition comprising SASPase polypeptides and the use of the composition for compensating for an imbalance in epidermal differentiation/proliferation such as regulating the phenomena of moisturization, inflammation, melanogenesis and/or desquamation, or treating dermatological disorders related to keratinization conditions. There are no indicia that the present application enables the full scope in view of the claimed method using the composition as discussed in the stated rejection. The present application does not provide teaching/guidance as to enable the full scope of the claims. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence

or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the homologs or the proteolytic peptide mixtures of SASPase polypeptides in the composition, and the effects of the composition, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no working examples indicating the use/effects of the composition in combating skin conditions associated with a dysfunction of cell proliferation and/or differentiation or treating a dermatological infection. Example XI merely shows the use of SEQ ID NO:6 in decreasing the percentage of residual corneodesmosin.

(3). The state of the prior art and relative skill of those in the art:

While the related art (e.g., Isogai *et al.*, U.S. Patent 6,979,557) teaches the full length nucleotide sequence of the cDNA of NT2NE20005500 and amino acid sequence encoded by the nucleotide sequence has been determined (see Table 1, SEQ ID NO:2323), and the amino acid sequence of SEQ ID NO:2323 containing 343 amino acids has 100% sequence identity to the sequence of SEQ ID NO:6 (see attached sequence match), the general knowledge and level of the skill in the art do not supplement the omitted description (i.e., the use/effects of the composition in treating skin conditions associated with a dysfunction of cell proliferation and/or differentiation), the specification needs to provide specific guidance on identities of the

homologs or the proteolytic peptide mixtures of SASPase polypeptides in the composition and their effects in the treatment to be considered enabling for the variant.

(4). Predictability or unpredictability of the art:

The specification has shown the use of SEQ ID NO:6 in decreasing the percentage of residual corneodesmosin. However, the specification has not demonstrated the use/effect of the composition comprising SASPase polypeptides or homologs or the proteolytic peptide mixtures of SASPase polypeptides in the treatment of skin conditions related dysfunction of cell proliferation and/or differentiation. The invention is highly unpredictable regarding the effect of the composition in the treatment.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method for combating skin conditions associated with a dysfunction of cell proliferation and/or differentiation or treating a dermatological infection, comprising administering the composition comprising an effective amount of at least one polypeptide of SEQ ID NO:4, 5 or 6, homologs thereof, or a mixture derived from the proteolysis of the polypeptide. The specification indicates a polypeptide having the sequence of SEQ ID NO:5 and isolated from human keratinocytes belongs to aspartic acid protease family (SASPase), where the polypeptide is autocatalytic and generates specific active form of SEQ ID NO:6 or active sequences of SEQ ID NO:16, 25 and 27 (pages 2-4; Examples I-IV) and the use of SEQ ID NO:6 in decreasing the percentage of residual corneodesmosin (Example XI). However, the specification has not demonstrated the use/effect of the composition comprising SASPase polypeptides or homologs or the proteolytic peptide mixtures of SASPase polypeptides

in the treatment of skin conditions related dysfunction of cell proliferation and/or differentiation. There are no working examples indicating the use/effect of the composition comprising SASPase polypeptides or homologs or the proteolytic peptide mixtures of SASPase polypeptides in the treatment of skin conditions related dysfunction of cell proliferation and/or differentiation. Since the specification fails to provide sufficient teachings on the use and effect of the composition in the treatment, it is necessary to carry out undue experimentation to identify a composition comprising the active SASPase polypeptide and to assess its effect in the treatment.

(6). Nature of the Invention

The scope of the claims encompasses a method of combating skin conditions associated with a dysfunction of cell proliferation and/or differentiation or treating a dermatological infection using a SASPase polypeptide, but the specification does not demonstrate the use and the effect of the composition comprising a SASPase polypeptide in the claimed method. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working example does not demonstrate the claimed methods associated with variants, the effect of the composition in treatment is unpredictable, and the teachings in the specification are limited, therefore, it is necessary to carry out undue experimentation to identify an active SASPase polypeptide and to assess its effect in the claimed method.

5. Claims 1-11 and 48-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-11 and 48-51 are directed to a cosmetic or pharmaceutical composition comprising at least one polypeptide of SEQ ID NO:4, 5 or 6 and homologs thereof; a cosmetic or pharmaceutical composition comprising at least one polypeptide mixture derived from the proteolysis of a polypeptide, the polypeptide sequence being SEQ ID NO:4, 5 or 6 and homologs thereof; and a method for combating skin conditions combating associated with a dysfunction of cell proliferation and/or differentiation or treating a dermatological infection, comprising applying to the skin the composition. While the specification indicates the present invention is related to a polypeptide having the sequence of SEQ ID NO:5 and isolated from human keratinocytes belongs to aspartic acid protease family (SASPase), where the polypeptide is autocatalytic and generates specific active form of SEQ ID NO:6 or active sequences of SEQ ID NO:16, 25 and 27 (pages 2-4; Examples I-IV) and the use of SEQ ID NO:6 in decreasing the percentage of residual corneodesmosin (Example XI), the specification does not disclose a genus of variants for homologs of SASPase polypeptides or for polypeptide mixture derived from the proteolysis of the SASPase polypeptides; and the use of these SASPase polypeptide variants in the treatment. Without guidance on structure to function/activity of SASPase polypeptide variants, one skilled in the art would not know which SASPase polypeptide variant is functional. A specific example of active form of SEQ ID NO:6 do not proved a sufficient written description for genus of variants of numerous SASPase polypeptide variants as encompassed by the claims. The lack of description on function/activity of SASPase polypeptide variants including homologs or peptide mixtures of proteolysis, and lack of representative species as encompassed by the

claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 5-11, 35 and 49-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 5 and 35 are indefinite because of the use of the term "a hydrophilic or hydrophobic targeting agent". The cited term renders the claim indefinite, it is not clear what target agent the term refers to.

8. Claims 6-11 and 49-51 are indefinite because of the use of the term "derived from". The cited term renders the claim indefinite, it is not clear how different the peptide mixtures derived from the proteolysis of the peptide are from the peptide mixtures after the proteolysis of the peptide. Claims 8, 9, 11 and 49-51 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend. Use of the term "obtained from" is suggested.

9. Claims 7-11, 50 and 51 are indefinite as to what outcome an effective amount of the polypeptide would produce. Claims 8, 9, 11, 50 and 51 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1, 2 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isogai *et al.* (U.S. Patent 6,979,557 B2)

Isogai *et al.* teach a cDNA derived from human such as NT2NE20005500 has been isolated, and the full length nucleotide sequence of the cDNA and amino acid sequence encoded by the nucleotide sequence has been determined (see Table 1, SEQ ID NO:2323), and the amino acid sequence of SEQ ID NO:2323 containing 343 amino acids has 100% sequence identity to the sequence of SEQ ID NO:6 (see attached sequence match). The reference also teaches the polypeptide encoded by the full-length cDNA can be prepared as a recombinant polypeptide or a natural polypeptide (column 29, lines 39-58; claim 28), and the polypeptides which may be involved in a disease are useful of developing a diagnostic marker or a medicine for regulation of their expression and activity, or as a target of gene therapy, thus the polypeptides can be formulated in a pharmaceutical composition (column 49, lines 14-28; column 64, line 65-column 65, line 20; claims 1-2). Although the reference does not specifically indicate the amino acid sequence of SEQ ID NO:2323 being isolated or used as a pharmaceutical composition, it does suggest the polypeptide can be recombinantly produced and used in a pharmaceutical composition. At the time of invention was made, it would have been obvious to one of ordinary skill in the art that the polypeptide of SEQ ID NO:2323 taught by Isogai *et al.* can be isolated

and prepared as a pharmaceutical composition because the cDNA encoding the polypeptide is isolated and the polypeptide can be produced recombinantly and tested, which results in the claimed invention and were, as a whole, prima facie obvious at the time the claimed invention was made.

Conclusion

11. Claims 1-11, 28, 35, and 48-51 are rejected; and claims 29-34, 46, 47 and 52 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Bragdon can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Primary Patent Examiner

CHIH-MIN KAM
PRIMARY EXAMINER

CMK
May 2 6, 2007

RESULT 1
US-10-094-749-2323
; Sequence 2323, Application US/10094749
; Patent No. 6979557
; GENERAL INFORMATION:
; APPLICANT: ISOGAI, TAKAO
; APPLICANT: SUGIYAMA, TOMOYASU
; APPLICANT: OTSUKI, TETSUJI
; APPLICANT: WAKAMATSU, AI
; APPLICANT: SATO, HIROYUKI
; APPLICANT: ISHII, SHIZUKO
; APPLICANT: YAMAMOTO, JUN-ICHI
; APPLICANT: ISONO, YUUKO
; APPLICANT: HIO, YURI
; APPLICANT: OTSUKA, KAORU
; APPLICANT: NAGAI, KEIICHI
; APPLICANT: IRIE, RYOTARO
; APPLICANT: TAMECHIKA, ICHIRO
; APPLICANT: SEKI, NAOHIKO
; APPLICANT: YOSHIKAWA, TSUTOMU
; APPLICANT: OTSUKA, MOTOYUKI
; APPLICANT: NAGAHARI, KENJI
; APPLICANT: MASUHO, YASUHIKO
; TITLE OF INVENTION: NOVEL FULL-LENGTH cDNA
; FILE REFERENCE: 084335/0160
; CURRENT APPLICATION NUMBER: US/10/094,749
; CURRENT FILING DATE: 2002-03-12
; PRIOR APPLICATION NUMBER: 60/350,435
; PRIOR FILING DATE: 2002-01-24
; PRIOR APPLICATION NUMBER: JP 2001-328381
; PRIOR FILING DATE: 2001-09-14
; NUMBER OF SEQ ID NOS: 3381
; SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 2323
; LENGTH: 343
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-094-749-2323

Query Match 100.0%; Score 708; DB 2; Length 343;
Best Local Similarity 100.0%; Pred. No. 2.6e-76;
Matches 138; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 ANSMGKGYYLKGKIGKVPVRFLVDSGAQVSVVHPNLWEEVTDGDLDTLQPFENVVKVANG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        189 ANSMGKGYYLKGKIGKVPVRFLVDSGAQVSVVHPNLWEEVTDGDLDTLQPFENVVKVANG 248

Qy         61 AEMKILGVWDTAVSLGKLKLKAQFLVANASAEEAIIGTDVLQDHNAILDFEHRTCTLKGK 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        249 AEMKILGVWDTAVSLGKLKLKAQFLVANASAEEAIIGTDVLQDHNAILDFEHRTCTLKGK 308

Qy        121 KFRLLPVGGSLEDEFDLE 138
              ||||||||||||||||||
Db        309 KFRLLPVGGSLEDEFDLE 326
```